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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,803	11/07/2001	Fernand Labrie	P/1259-637	3989

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EXAMINER	
CHONG, YONG SOO	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
04/29/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/052,803	LABRIE, FERNAND	
	Examiner	Art Unit	
	YONG S. CHONG	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/14/08*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,13-19,22-24,35-41 and 44* is/are pending in the application.

4a) Of the above claim(s) *24 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 13-19, 22-23, 35-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/14/2008 has been entered.

Claims 3-12, 20-21, 25-34, 42-43 have been cancelled. Claims 1-2, 13-19, 22-24, 35-41, 44 are pending. Claims 24 and 44 have been withdrawn. Claims 1-2, 13-19, 22-23, 35-41 are examined herein.

Applicant's arguments have been fully considered but found not persuasive. The rejections of the last Office Action are maintained for reasons of record and repeated below for Applicant's convenience.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Simard et al. (International Journal of Cancer (1997), 73(1), 104-112, "83" in PTO-1449 submitted November 7, 2001) for reasons of record stated in the Office Action dated February 8, 2005.

Simard et al. discloses a composition comprising 1713-estradiol (E2), the instant estrogen, and a simultanoues incubation with EM-652 or EM-800, the instant SERM compound, and a pharmaceutical diluent or carrier such as ethanol and water in vitro. See abstract, page 104-105; Fig 2-12 at page 106-111. Thus, the testing results show

that EM-652 or EM-800 as non-steroidal antiestrogens are useful in treating breast cancer in patients (see abstract), particularly including those woman patients who need to take estrogens daily for hormone replacement therapy (HRT).

Claims 1-2 and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Couillard et al. ("8" in PTO-1449 submitted November 1, 2004) for reasons of record stated in the Office Action dated February 8, 2005.

Couillard et al. discloses that administering estrone, the instant estrogen, to mice while co-administering EM-800 and DHEA in a composition with a pharmaceutical diluent or carrier, is useful in inhibiting breast tumors or cancer growth in mice.

Response to Arguments

Applicant argues that the Simard and Couillard references do not disclose a "pharmaceutical dosage form." At the outset, there is no explicit limitation in the claims reciting a "pharmaceutical dosage form." Examiner notes that Applicant has not filed an amendment to the claims on 6/22/2007 as argued in the last response. Moreover, this is not persuasive because Simard clearly disclose ethanol as a pharmaceutical carrier (pg. 105, right col. 2nd paragraph), therefore rendering the composition in a finished form suitable for administration to a patient. With regard to the Couillard reference, Examiner notes that once the active agents are administered to a patient, the composition is in contact with water in the blood.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 17-19, 22-23, and 35-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simard et al. or Couillard et al. for reasons of record stated in the Office Action dated February 8, 2005.

The same disclosure of Simard et al. or Couillard et al. has been discussed in the 102(b) rejection set forth above.

The prior art does not expressly disclose the employment of a kit to store the compositions of Simard et al. or Couillard et al. The prior art does not expressly disclose the employment of the known pharmaceutically acceptable salt of the acid in a pharmaceutical composition or a kit.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ a kit for comprising the composition of Simard et al. or Couillard et al. and to employ the known pharmaceutically acceptable salt of the acid in a pharmaceutical composition or a kit, since the patient pack or kit and the pharmaceutically acceptable salts are all deemed obvious; they are all within the knowledge and conventional skills of pharmacologist to conveniently assist the user and prescriber for easy dispensary of the medication.

Claims 1-2, 13-19, 22-23, and 35-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Luo et al. ("54", PTO-1449 submitted November 7, 2001) and Barrett-Connor et al. ("4", PTO-1449 submitted November 7, 2001), and Do Nascimento (of record) in view of Labrie et al. (WO 96/26201, PTO-1449 submitted November 7, 2001), for the same reasons of record in the Office Action dated February 8, 2005.

Luo et al. discloses that an estrogen, DHEA alone, or the particular SERM (antiestrogen), EM-800 alone (having 2S configuration and moieties convertible in vivo to hydroxyl), is known to be useful in a method of treating hyperlipidemia by decreasing serum lipid levels such as triglyceride and cholesterol levels. See abstract and page 4436 Fig. 1 "Structure of EM-800", page 4438 the left column "Effect on serum lipid levels". Luo et al. further discloses that the combination of DHEA and EM-800 exerts more potent effect on reducing serum lipid levels than each compound used alone (page 4438 the left column "Effect on serum lipid levels" and page 4439 Fig. 4, and page 4443 the left column.

Barrett-Connor et al. teaches that SERMs are capable of lowering serum lipid levels to reduce the risk of coronary heart disease, as estrogen does. See abstract.

Do Nascimento teach that the particular estrogen, 1713-estradiol, is useful in treating hypercholesterolemic patients (see abstract).

The prior art does not expressly disclose the employment of the combination of an estrogen such as 1713-estradiol and the particular SERM, EM-652.HCI, or further combining with DHEA in a pharmaceutical composition.

Labrie et al. (WO 96/26201) discloses that both EM-800 and EM-652 or EM-652.HCI are antiestrogens (SERMs), and EM-800 has moieties convertible in vivo to hydroxyl to become EM-652. Thus, EM-800 is a metabolite of EM-652, having the same functional property and activity.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ of the combination of an estrogen such as 1713-estradiol and the particular SERM, EM-652.HCI, or to further combine with DHEA, in a pharmaceutical composition.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the combination of an estrogen such as 1713-estradiol and the particular SERM, EM-652.HCI, or to further combine with DHEA, in a pharmaceutical composition, since estrogens such as 1713-estradiol and DHEA are well known in the art to be used in methods of treating hyperlipidemia by decreasing serum lipid levels such as triglyceride and cholesterol levels according to the cited prior art herein. Moreover, the particular SERM, EM-800, a known metabolite of EM-652

(convertible in vivo to hydroxyl to become EM-652), alone or in combination with an estrogen such as DHEA, is known to be useful in a method of treating hyperlipidemia by decreasing serum lipid levels such as triglyceride and cholesterol levels according to Luo et al.

Therefore, one of ordinary skill in the art would have reasonably expected that combining an estrogen such as 1713-estradiol and the particular SERM, EM-652.HCI, or further combining with DHEA, all known useful for the same purpose, i.e., treating hypercholesterolemia, would improve the therapeutic effects for treating the same disorder, hypercholesterolemia, and/or would produce additive therapeutic effects in treating the same. See In re Kerkhoven, 205 USPQ 1069 (CCPA 1980) regarding combination inventions. It is considered prima facie obvious to combine two active composition components into a single composition to form a third composition useful for the very same purpose.

"It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... The idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Further, the teachings of Luo et al. that the combination of DHEA and EM-800 exerts more potent effect on reducing serum lipid levels than each compound used alone clearly provides the motivation of the instant claimed method employing the combination of EM-652, 17-estradiol and DHEA.

Furthermore, one of ordinary skill in the art would have been motivated to prepare a kit comprising the same composition because the preparation of a kit comprising a pharmaceutical composition is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

Thus the claimed invention as a whole is clearly prima facie obvious over the teachings of the prior art.

Response to Arguments

Applicant argues "both Simard and Couillard teach aqainst estrogen. Couillard notes at abstract lines 6-7, "Estrone caused a 10-fold increase in ZR-75-1 tumor area..." ZR-75-1 is defined as human mammary tumor. Likewise, Simard states that estrogens play a predominant role in the development and growth of human breast cancer..." (abstract, lines 1-2).

Applicant's argument is not found persuasive. Since first, the instant claims are directed to a pharmaceutical composition, which is a product claim not method claim. Thus, so long as Simard et al. discloses a composition comprising 17~-estradiol (E2), the instant estrogen, and a simultanoues incubation with EM-652 or EM-800, the instant SERM compound, and a pharmaceutical diluent or carrier such as water in vitro, or Couillard et al. discloses that administering estrone, the instant estrogen, to mice while co-administering EM-800 and DHEA in a composition with a pharmaceutical diluent or carrier, the prior art reads on the claimed composition.

Applicant argues against the use of In re Kerkhoven case law since both Barret-Conner and Labrie fail to address cholesterol levels in the context of treating hypercholesterolemia.

This is not persuasive because hypercholesterolemia is defined as higher than normal levels of cholesterol in the blood. Since cholesterol is a lipid, Barret-Conner's teaching that SERMs are capable of lowering serum lipid levels, is viewed as addressing cholesterol levels. Furthermore, Labrie was only used to show that both EM-800 and EM-652 or EM-652.HCI are antiestrogens (SERMs), and that EM-800 has moieties convertible in vivo to hydroxyl to become EM-652. The In re Kerkhoven case law was used in the obviousness rejection to show that the teachings in the Luo, Barret-Connor, and Do Nascimento references are all used for the same purpose.

Therefore, one of ordinary skill in the art would have reasonably expected that combining an estrogen such as 1713-estradiol and the particular SERM, EM-652.HCI, or further combining with DHEA, all known useful for the same purpose, i.e., treating hypercholesterolemia, would improve the therapeutic effects for treating the same disorder, hypercholesterolemia, and/or would produce additive therapeutic effects in treating the same.

Applicant argues that Luo does not disclose DHEA as an estrogen. Moreover, the estrogens within the scope of claim 1 do not include DHEA.

This is not persuasive because Luo clearly teaches the use of EM-800, which is the estrogen as claimed in claim 1. The fact that Luo also disclosed DHEA is irrelevant,

especially since Applicant uses the open transitional phrase "comprising" and the fact that DHEA is not precluded in the instant invention.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

YSC

/SREENI PADMANABHAN/
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